REMARKS

By this Amendment claims 5 and 24 have been amended to address and overcome the examiner's rejection thereagainst under 35 U.S.C. 112. Entry is requested.

In the outstanding Office Action the examiner has rejected claims 1, 2, 4-6, 24 and 25 under 35 U.S.C. 103(a) as being unpatentable over Hiestand et al. in view of Barnett et al. (newly cited), Macauley and Wheeler.

The applicants assert that this rejection is without merit.

Hiestand et al. has been discussed previously. The examiner acknowledges that there is no disclosure in Hiestand et al. of (i) biliquid foams (polyaphron dispersions); (ii) the size of the particle; and (iii) the droplet size of the biliquid foam.

Barnett et al. teach drug loaded polyaphrons (biliquid foams). In particular, this patent discloses polyaphrons at least two fluid phases; a first continuous phase and a second dispersed phase. The dispersed phase includes a substance which may be transferred to another medium. Barnett et al. also mention a polyaphron droplet size range of 1 micron to 1mm. It is noted that Barnett et al. are silent on powders. Moreover, the patent is silent on particles having a specified size.

It is submitted that there would be no motivation to combine the teaching of Barnett et al. with that of Hiestand et al.

The problem to be solved having regard to Hiestand et al. is to provide a powder which has improved properties for use as a controlled release system.

The combination of the use of (i) biliquid foams (polyaphron dispersions); (ii) the size of the particle; and (iii) the droplet size of the biliquid foam leads to the powders of the present invention having the unexpected advantage that even after the powder has been compressed into a tablet, and the oil droplets are subsequently released from the powder by dissolution of the polymer, the oil droplets size distribution is substantially unaffected (see Example 12).

When looking to provide a powder having improved properties for use as a controlled release system, there would be no motivation to consider Barnett et al. Barnett et al. are silent on powders. Thus, a person of ordinary skill would not consider this patent to be of relevance. If the person of ordinary skill did consider this patent, it is noted that it provides very limited instructions on the preparation of biliquid foams and no formal examples. Moreover, this patent suggests that in some circumstances biliquid foams are unstable in the systems of Barnett et al. Column 2, lines 33 to 35, of the Barnett et al. patent states that "however, the systems were not appreciably stable for any significant

period of time with the exception of the peanut and mineral oils". Column 3, lines 19 to 22 (referring to mineral oil) states "one problem experienced with the polyaphrons was that over a period of time, particularly at 37 degrees centigrade, there was some coalescence of oil at the air/polyaphron interface". Barnett et al. further describe that these polyaphrons are subject to interfacial instabilities (see column 3, lines 24 and 25). It is therefore submitted that the person of ordinary skill in the art, far from being motivated to combine the teaching of Barnett et al. and Hiestand et al., would be dissuaded from doing so as Barnett suggests there is no long term stability of the polyaphrons described in this patent. At best, Barnett et al. suggest that in order to obtain stable systems, there will be a limitation on the choice of oils (peanut and mineral oil only).

Barnett et al. suggest that the long term stability of the systems may only be helped by the reaction of monomers to form a polymerized polyaphron system. However, no evidence for this is shown. Moreover, it is noted that where Barnett et al. teach the addition of monomers to either the dispersed or continuous phase, the polymerization of these monomers acts as thickeners which are used to mediate the passage of the drug from the polyaphron into the continuous phase. The examiner (on page 8 of his Office Action) states that Barnett et al. expressly suggest that a polymer matrix may be formed about the outside of the

polyaphron in order to precisely control the release rate of the drug dispersed therein. The examiner also states that these compounds are referred to as thickening agents. However, Barnett et al. do not teach that the polyaphrons are entrapped in a polymer matrix to form a discrete powder. Instead, Barnett et al. only teach thickening either or both of the dispersed or continuous phases. There is no disclosure in this patent of dried or discrete powder systems.

In view of the foregoing a person of ordinary skilled in that art would be dissuaded from combining the teachings of Hiestand et al. and Barnett et al.

Furthermore, even a person of ordinary skill combined the teaching of Hiestand et al. in combination with Barnett et al. in the light of Macauley and Wheeler, he would not arrive at the present invention.

Barnett et al. disclose a polyaphron dispersion wherein the disperse phases of the droplets have a mean diameter size between 1 micron to 1mm (see claim 1). The present invention requires that the biliquid foam droplets have a mean size of 1 to 45 microns.

The examiner has suggested that it is customary for an artisan of ordinary skill to adjust the sizes of both the droplet and overall particle of the composition. However, Barnett et al. teach in the systems described in the patent that the stability of polyaphrons is not appreciable and that the polyaphrons are subject to coalescence. A person of ordinary skill in

the art would know that reducing droplet size further would result in higher surface area and therefore lower stability at a given surfactant level. Therefore, the motivation from this teaching would not lead to the current invention. In the present invention, a low level surfactant is used (preferably 0.1 to 1 % wt/wt on total biliquid foam) and a low droplet size (1 to 45 microns and preferably below 12 microns) is used to generate stable systems (see example 12 where the compression of the powder does not affect the redispersion of the oil droplets upon dissolution in deionised water and the droplet size distribution appeared unaffected). In the extensive examples given in the present application a range of different oils are used and not limited to mineral oil and peanut oil.

A person of ordinary skill would be aware that the maintenance of droplet size on dissolution is important in systems such as pharmaceutical formulations. Moreover, the stability of a given system is also important. In view of this, the motivation to use the teaching of Barnett would be limited.

It is also noted that the teaching of Barnett et al. which warns of the potential coalescence of polyaphrons would not motivate the artisan to use high shearing methods (such as spray drying) to provide polyaphrons (biliquid foams) having a small droplet size.

In view of the foregoing, even if a person of ordinary skill combined the teachings of Hiestand et al. and Barnett et al. in the light of Macauley and Wheeler, he would not arrive at the present invention.

Favorable reevaluation is requested.

Respectfully submitted,

DYKEMA GOSSETT PLLC

By: _____

Richard H. Tushin
Registration No. 27,297
Franklin Square, Third Floor West
1300 I Street, N.W.
Washington, DC 20005-3353
(202) 906-8680